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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,775	06/30/2006	Georg Feger	ARS-117	1797
23557 7590 01/31/2008 SALIWANCHIK LLOYD & SALIWANCHIK A PROFESSIONAL ASSOCIATION PO BOX 142950 GAINESVILLE, FL 32614-2950			EXAMINER MACFARLANE, STACEY NEE	
			ART UNIT 1649	PAPER NUMBER
			MAIL DATE 01/31/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/550,775

Applicant(s)

FEGER ET AL.

Examiner

Stacey MacFarlane

Art Unit

1649

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26-43 is/are pending in the application.
- 4a) Of the above claim(s) 28-31 and 40-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 26, 27 and 32-39 is/are rejected.
- 7) ☒ Claim(s) 34 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 September 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☒ Other: 2 pages attached.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I and the species of "traumatic nerve injury of the peripheral nervous system" in the reply filed on November 19, 2007 is acknowledged.
2. Claims 28-31 and 40-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 19, 2007.

Claims 26, 27, and 32-39 will be examined in the instant office action.

Claim Objections

3. Claim 34 is objected to because of the following informalities: Claim recites dependency from itself. Appropriate correction is required.

Drawings

4. This application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no sequence identification has been provided for the amino acid sequence presented in Figure 1 of the instant specification. In case this sequence is new, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same

and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. See M.P.E.P. 2422.04.

Specification

5. The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (for example, see page 8 of the instant specification). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 26, 27 and 32-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 26 is vague and indefinite in so far as it employs the term "clusterin" as a limitation. This term is appears to be novel, and without a reference to a precise amino

acid sequence identified by a proper SEQ ID NO: one cannot determine the metes and bounds of "clusterin". Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of "clusterin", an artisan cannot determine if a compound would be included or excluded from the claimed subject matter by the presence of this limitation.

9. Claims 26 and 27 are vague and indefinite in their recitation of prevention of the instantly-elected traumatic nerve injury of the peripheral nervous system. Absent the method steps by which the process is performed, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the method.

10. Claim 26 is further vague and indefinite in its recitation of an agonist or activity, absent a specified activity, one of ordinary skill in the art would not know the metes and bounds of the claim.

11. Claim 26 is vague and indefinite in its recitation of "isoforms" and "derivatives", absent a recitation within the specification as to the distinguishing features of the different isoforms over the different derivatives, an artisan would not be reasonably apprised as to the subject matter claimed.

12. Claim 34 recites the limitation "the fused protein" in claim 34. There is insufficient antecedent basis for this limitation in the claim.

13. Claims 37 and 39 are vague in their recitation of "use" or "used". Without active steps delineating the specific use, it is unclear if the Applicant is reciting a use that is known in the art or one that is a novel feature of the invention. A recitation of "administration" would obviate this rejection.

14. Claims 32-33, 35-36 and 38 are indefinite for depending from indefinite claims.

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 26, 27, and 32-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 26 recites a composition comprising clusterin, an isoform, mutein, fused protein, functional derivative, active fraction, circularly permuted derivative, or an agonist of clusterin activity. Claim 32 recites sequences with "at least 40 % or 50 % or 60 % or 70 % or 80 % or 90 % identity" to SEQ ID NO: 1 or any of its fragments. Claims 27, and 33-39 are dependent claims and are therefore included in the rejection. The claims do not require that the "isoform, mutein, fused protein, functional derivative, active fraction, circularly permuted derivative, or an agonist of clusterin activity" or mutein having "at least 40 % or 50 % or 60 % or 70 % or 80 % or 90 % identity" to SEQ ID NO: 1 or any of its fragments, possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of molecules defined only as being related to clusterin or having agonist clusterin activity, therefore

the genus is merely defined by name and function and the instant specification fails to describe the entire genus of molecules that are encompassed by these claims.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of specific examples of clusterins (§s 0077 and 0078 of the PGPub). The claims, however, encompass method of administration of any clusterin isoform, mutein, fused protein, functional derivative, active fraction, circularly permuted derivative, or an agonist of clusterin activity, thus, the claims are not limited to specific molecules with known structure. The claims merely require the claimed methods employ molecules that serve to activate clusterin activity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claims is a recitation of a name, "clusterin" and a reference to limited similarity to SEQ ID NO: 1 or fragments thereof. Moreover, the specification states that "Despite its ubiquitous expression ... the genuine function of clusterin remains unraveled" (§ 0035). Therefore, it is not even known what activity the clusterin isoform, mutein, fused protein, functional derivative, active fraction, circularly permuted derivative, or an agonist is meant to

exhibit. Furthermore, there is not even identification of any particular portion of the structure that must be conserved for activity. As stated above, it is not even clear what molecules except that of SEQ ID NO: 1 would serve as a form of clusterin or as an agonist/activator. The specification does not provide a structure of these isoforms, muteins, fused proteins, functional derivatives, active fractions, circularly permuted derivatives, or agonists, and fails to provide a representative number of species for the recited genus (i.e. a representative number of molecules having at least 40, 50, 60, 70, 80 or 90% homology to SEQ ID NO: 1 AND having a relevance to clusterin activity). Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, the court clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the structure of the encompassed genus of clusterin isoforms, muteins, fused proteins, functional derivatives, active fractions, circularly permuted derivatives, or an agonists, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identifying activity. Adequate written description requires

more than a mere recitation of activity as part of the invention and a reference to a potential method of isolating or screening. The compound itself is required. See *Fiers v Revel*, 25 USPQ2d 1601 at 1601 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification only provided for the bovine sequence.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

18. Claims 26, 27, 32 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Fiscella et al. US 2003/0017297 A1, published February 6, 2003.

19. Claim 26 is drawn to a method of preventing or treating a peripheral neurological disease comprising the administration of a composition comprising administering clusterin to an individual having peripheral neurological disease. Dependent claims recite wherein the peripheral neurological disease is the instantly-elected traumatic nerve injury of the peripheral nervous system (Claim 27), wherein the clusterin is a mutein polypeptide comprising at least 40% identity to SEQ ID NO: 1 (Claim 32), and administration of about 0.001 to 100 mg/kg or body weight or about 1 to 10 mg/kg of body weight or about 5 mg/kg of body weight (Claim 39).

20. The Fiscella et al. reference teaches administration of a polypeptide (SEQ ID NO: 34 of the reference) that is 57.6% identical to SEQ ID NO: 1 of the instant claims (see alignment attached) for the treatment of traumatic injury of both the central and peripheral nervous systems (column 139, lines 4-55). Thus, teaching a mutein of SEQ ID NO: 1 wherein the amino acid sequence has at least 40% identity to the instantly claimed subject matter. Furthermore, the reference teaches polypeptides are administered in the range of 1 µg/kg body weight to 10mg/kg body weight (column 212, lines 18-19), which teaches the limitation of administration of "about 0.001 to 100 mg/kg or body weight or about 1 to 10 mg/kg of body weight or about 5 mg/kg of body weight" as recited in instant Claim 39. Therefore, instant claims 26, 27, 32 and 39 are anticipated by the reference.

21. Claims 26 and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by PCT/US02/40892, filed December 23, 2002.

22. Claims 26 and 32 are drawn to a method of preventing or treating a peripheral neurological disease comprising the administration to an individual having peripheral neurological disease of a composition comprising an active fraction or fused protein of a clusterin wherein the clusterin is SEQ ID NO: 1.

23. PCT/US02/40892 teaches albumin fusion proteins comprising amino acid residues 1-22 of SEQ ID NO:1 (see SEQ ID NO:382 of reference) for the treatment and prevention of diabetic neuropathy (column 2, lines 27-13 and column 5, lines 2-4). The instant specification defines diabetic neuropathy as falling within the peripheral neurological diseases of the instant claims (see ¶ 0091). Therefore, the reference anticipates the method of claims 26 and 32.

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

25. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

26. Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fiscella et al. as applied to claims 26, 27, 32 and 39 above, and further in view of Koch et al. Prostate Cancer and Prostatic Diseases 1:101-104, published 1997.

27. Claim 35 is drawn to the method of preventing or treating a peripheral neurological disease comprising the administration of a composition comprising clusterin wherein the composition further comprises heparin.

28. The Fiscella et al. reference teaches administration of a clusterin polypeptide, which is at least 40% homologous to the instantly-claimed clusterin polypeptide of SEQ ID NO: 1, for the treatment of traumatic injury of both the central and peripheral nervous systems and teaches the limitation of claim 26. The Fiscella reference does not teach a composition further comprising heparin as recited by claim 35. The Koch et al. reference teaches that heparin is a useful treatment following radical prostatectomy (whole reference) and the instant specification defines surgical prostatectomy as a specific embodiment of traumatic nerve injury of the PNS (¶ 0006).

29. Section 2144.06 of the MPEP outlines the examination of Art Recognized compositions useful to treat the same condition and quotes, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been

individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In the instant case, the Fiscella prior art has taught that clusterin polypeptides are useful for the treatment of peripheral neurological disease and the Koch prior art teaches that heparin is useful for the treatment of peripheral neurological disease following radical prostatectomy. Thus, it would have been obvious to one of ordinary skill to combine the teachings and compositions as taught by the reference for a combined method of treating peripheral neurological disorders because it the art has recognized their usefulness for that same purpose.

30. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fiscella as applied to claims 26, 27, 32 and 39 above, and further in view of DiPaola et al., *Clinical Cancer Research*, 3:1999-2004, November 1997.

31. Claim 37 is drawn to the method of preventing or treating a peripheral neurological disease comprising the administration of a composition comprising clusterin wherein the composition further comprises an interferon for simultaneous, sequential or separate use. The instant specification defines surgical prostatectomy as a specific embodiment of traumatic nerve injury of the PNS (¶ 0006).

The Fiscella et al. reference teaches administration of a clusterin polypeptide, which is at least 40% homologous to the instantly-claimed clusterin polypeptide of SEQ ID NO: 1, for the treatment of traumatic injury of both the central and peripheral nervous systems and teaches the limitation of claim 26. The Fiscella reference does not teach a composition further comprising interferon as recited by claim 37. The DiPaola et al.

reference, however, teaches that compositions comprising interferon are useful treatment following radical prostatectomy (abstract) and the instant specification defines surgical prostatectomy as a specific embodiment of traumatic nerve injury of the PNS (¶ 0006).

Section 2144.06 of the MPEP outlines the examination of art recognized compositions useful to treat the same condition and quotes, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In the instant case, the Fiscella prior art has taught that clusterin polypeptides are useful for the treatment of peripheral neurological disease and the DiPaola prior art teaches that interferon is useful for the treatment of peripheral neurological disease following radical prostatectomy. Since it is *prima facie* obvious to combine two compositions each of which is known to be useful for the same purpose, the invention as a whole is *prima facie obvious*, if not actually anticipated by the reference.

Conclusion

32. No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on M,W and ALT. F 6 am to 3 pm, T & R 5:30 am - 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/SNM/


OLGA N. CHERNYSHEV, PH.D.
PRIMARY EXAMINER

Page 15

Query Match 57.6%; Score 1360; DB 3; Length 363;
Best Local Similarity 74.6%; Pred. No. 2.7e-107;
Matches 252; Conservative 39; Mismatches 45; Indels 2; Gaps 1;

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; Sequence 34, Application US/10733368
; Publication No. US20040126801A1
; GENERAL INFORMATION:
; APPLICANT: Fiscella et al.
; TITLE OF INVENTION: 19 Human secreted proteins
; FILE REFERENCE: PZ045P1
; CURRENT APPLICATION NUMBER: US/10/733,368
; CURRENT FILING DATE: 2003-12-12
; PRIOR APPLICATION NUMBER: US/09/832,129
; PRIOR FILING DATE: 2001-04-11
; PRIOR APPLICATION NUMBER: PCT/US00/28664
; PRIOR FILING DATE: 2000-10-17

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Page 16

Query Match 57.6%; Score 1360; DB 4; Length 363;
Best Local Similarity 74.6%; Pred. No. 2.7e-107;
Matches 252; Conservative 39; Mismatches 45; Indels 2; Gaps 1;

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Db	1	MKTLLLVGLLLLWENGRVLGDQMVSDELQEMSTEGSKYINREIKNALKGKVIKTLIE	60
Qy	62	KTNEERKTLNLSNEEAKKKEDALNETRESETKLKELPGVCNETMMALWEECKPCLKQTC	121
		: : : : :	
Db	61	QTNEERKSLLTNLEEAKKKEDALNDTKDSEMMLKASQGVCNDTMMALWEECKPCLKQTC	120
Qy	122	MKFYARVCRSGSLVGRQLLEEFNLQSSPFYFWMNGDRIDSLLENDRQQTHLDMVMQDHFS	181
		: : :	
Db	121	MKFYARVCRSSTGLVGHQVEEFNLQSSPFYFWINGDRIDSLLENDRQQTHALDMVQDSFD	180
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Qy	242	AMFQPFLMIHEAQQAMDIFHSPAFQHPPTFEIREGDDRTVCREIRHNSTGCLRMDQ	301
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Qy	302	CDKCREILSVDCSTNNPSQAKLRRELDESQVAERLTR	339
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